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VENEREAL DISEASES FROM THE EPIDEMIOLOGICAL POINT OF VIEW

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LADIES AND GENTLEMEN,—I should like to begin by thanking you very cordially for the honour which you have done me in electing me President of this Society. It was with diffidence that I accepted the position, in view of the great distinction of those who have held this office before me, and in view also of the fact that I have no pretensions to a clinical knowledge of venereal disease. I feel that, coming among experts and specialists in this work, I occupy a somewhat false position as President of the Society. But I assure you of my great interest in the Society and my admiration for the work it is doing in improving the outlook on the treatment of venereal diseases. I take it that the reason you asked me to occupy this position was that, as an Officer of the Ministry of Health, I am closely associated with the work of venereal disease clinics, in which many of the members of the Society are engaged. I fully recognise the value of the work which is being done, and I have always felt gratified at what I consider to be the remarkable success of the treatment of venereal diseases as carried out in those centres. In my view, there are few directions in which expenditure of money on public health has produced such valuable results in proportion to the cost.

As I could not think of talking to you on a clinical subject, I found considerable difficulty in coming to a conclusion as to my topic for to-night's address, but I hope the subject eventually chosen may present some points of interests: "Venereal Diseases from the Epidemiological Point of View."

Of the evolution of man we have learned a good deal during the last century, but with regard to the evolution of the parasites of man, and particularly those microscopic

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organisms associated with the production of disease in man, we are still profoundly ignorant.

That evolutionary processes have been at work in connection even with such low forms of life seems certain. We take it for granted that pathogenic organisms have been developed from harmless saprophytes of similar structure and mode of growth. Again, we know that pathogenic organisms vary in virulence, and such changes must be associated with some modifications still obscure to us in the life-history of the parasite and in its reaction to its environment.

There can be little doubt, I think, from our knowledge of other animals, that man has inherited at least some of his parasites from lower forms of animal life from which he is descended. Possibly some of these parasites had developed pathogenic properties before man became differentiated as a separate species. The fact that certain pathogenic organisms of very closely allied type produce diseases of more or less similar character in animals and in man suggests this possibility. For instance, forms closely allied to the human tubercle bacillus produce disease in fish, in birds and in cattle. It is, of course, possible on the other hand that some harmless parasite developed independently in different groups of animals and thus produced the avian, bovine and human type of tubercle bacillus.

The fact that certain pathogenic organisms of man are not pathogenic to other animals suggests, although it does not necessarily prove, that the parasites responsible for certain diseases in man developed their pathogenic properties at some period subsequent to man's separation as a distinct species.

The whole subject of parasitism is of great interest, but it would lead us too far afield to speculate as to why certain forms, instead of leading an independent existence, became intimately associated with the life-history of other organisms. There can be little doubt, however, that at a very early period of the development of animal life parasites appeared. There seems reason to believe that in some instances this symbiosis was useful to both parasite and host. In some cases the presence of the parasite apparently produces neither a beneficial nor an inimical effect on the host.

It seems difficult to understand why a parasite should

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develop pathogenic properties, even to the extent of such virulence as to kill its host. From the point of view of survival of the race it would not seem to the advantage of the parasite that the process of acquiring virulent pathogenic properties should proceed too far. If virulence is so much enhanced that the host is promptly killed off, it is clear that there is a probability that the parasitic family may come to an untimely end before they can be successfully transferred to new victims. It is true that certain organisms have overcome this difficulty by the evolution of a "spore," or resting form, so that from the dead bodies of victims of the disease infection may be spread to other animals of the host species, *e.g.*, anthrax.

In the case of animals a plague caused by an organism of excessive virulence might conceivably sweep off the whole herd, the race of virulent parasites coming to an end contemporaneously with the extermination of the herd.

In the case of primitive man it is possible that extermination of isolated communities may actually have taken place, but when man had reached a higher level of intelligence, probably long before such a disaster could occur, panic would dictate the application of drastic and possibly even cruel measures of exclusion or segregation of the infected units, and possibly also of those who had been closely in contact with infected cases.

With regard to certain parasites it would appear that a state of tolerance is set up between the parasite and the host, for instance, the normal saprophytes of the nose and throat and of the intestines. Even with regard to some of these, however, we know that virulence of the parasite may be increased to the point of causing danger to the host, *e.g.*, in the case of the *Bacillus coli*.

In the case of other parasites there seems to be a constant struggle between the powers of attack of the parasite and the powers of defence of the host. Increased virulence of an organism will probably enable the attack of the parasite on a new host to be more successful, *i.e.*, a smaller dose of infection may effect a successful invasion of a host whose natural resistance may be sufficient to deal with a similar dose of lesser virulence.

We know of three modes of transmission of parasites of infectious diseases :—

(1) Direct contagion. The venereal diseases are outstanding examples of this mode.

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(2) Direct transmission by means of air, water, food, etc. Examples of this mode are influenza, pneumonic plague, cholera and smallpox.

(3) Indirect transmission, *i.e.*, by means of an intermediate host, *e.g.*, malaria.

It would appear probable that parasites of the first type are the most primitive group of parasites responsible for infectious diseases. Syphilis and soft chancre are regarded by Gill¹ as prototypes of this primitive group of diseases, whose persistence in their present form and whose world-wide distribution may be accounted for by the fact that a mode of transmission dependent upon so fixed an instinct as reproduction is eminently calculated to ensure the survival of the *materies morbi* in all circumstances and throughout all time.

Andrewes² states that we must assume that the infecting agent of syphilis was a harmless genital saprophyte which acquired parasitic powers enabling it to invade living tissues.

Warthin³ suggests that certain deep-seated biologic differences between women and men in the reaction to the presence of the *Treponema pallidum* may possibly be due to the parasite being the pathogenic descendant of some harmless spirochætal form inhabiting the female body ages ago.

As prolonged time would probably be necessary to enable a harmless saprophyte of the genital organs to assume the pathogenic properties of *Treponema pallidum*, Gill would relegate the origin of diseases associated with human parasites to a very early period in the history of the human race.

The gonococcus is similarly assumed to have been originally a harmless coccus inhabiting the genital tract which developed pathogenic properties in a very distant age. Similarly with the organism of soft sore.

Several writers agree in thinking that circumstances would not be favourable for the evolution of pathogenic organisms until the increase in numbers of men and change of mode of life led to congestion or overcrowding. In such circumstances economic pressure would tend to lower resistance. Increased association of human beings with certain organisms and decreased powers of resistance might have been the first stage in the evolutionary history of epidemic diseases.

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As Gill¹ points out, on this view, epidemics of disease constituted the means by which Nature sought to place a check upon the multiplication of man beyond the limit of his food supply.

Since man has been the victim of infectious diseases from a very early period in the history of the race, and since such diseases are particularly liable to occur in epidemics or localised outbreaks of considerable severity, it is certain that mankind made a study of them a long time ago. Epidemiology, which has been defined as the study of what may be termed the natural history of infective disease, has therefore a very ancient origin, but it must be confessed that it cannot yet be looked upon as an exact science, and the progress of our knowledge has been very slow. As Singer⁴ says, we are completely ignorant on two most important points, viz., how infective disease first began, and secondly, "why diseases distributed over a wide area and in many bodies should vary in virulence from time to time; why, for instance, a relatively mild condition, such as influenza, should suddenly devastate the world."

In ancient times the influence of evil spirits or the wrath of the gods was considered to account for pestilences, and even in the fifteenth century the violent outbreak of syphilis was called the "flagellum Dei," or the "scourge of God."

The Greek theory with regard to epidemics was that three factors were involved: two peculiar to the individual, viz., temperament and habits of life, and a third an extra-corporeal factor affecting the community—the atmospheric or telluric status. Hence arose the miasmatic theory, which held the field for many years, and was modified and amplified by Sydenham, who revived and extended the Hippocratic teaching as to "epidemic constitutions," but thought it was rather the "occult" than the perceptible changes of the atmosphere which led to outbreaks of infectious disease (Gill).

It is worthy of note, however, that one writer a century before the time of Sydenham had already conceived the idea of a living *contagium*, capable of propagation, as being a cause of transmission of infection. This was Hieronymus Fracastoro, whose name will ever be remembered because from the name of a figure in his poem, "Syphilidis Libri III.," published in 1530, was derived

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the name given to the disease "Syphilis," which had raged so violently in Europe during the early years of that century.

He was, of course, not the first to recognise that diseases spread from person to person, but he believed that this occurred through the transmission of "*seminaria*," living particles which possessed the power of propagating and begetting their like. He ridiculed the idea of occult influences being concerned.

It is particularly interesting to this Society, whose object is the study of venereal diseases, that it was the physician to whose writings we owe the name of "*Syphilis*" who appears to have been the first to enunciate clearly the "germ theory" of disease. His ideas on this point fell on stony ground, and it was left for the genius of Pasteur and Koch to place on a firm basis the causal relation of micro-organisms to disease. Their work naturally profoundly influenced the consideration of the problems of epidemics of infectious disease, and there has been a tendency to study each disease in the light of our knowledge of the individual parasite concerned and to try and explain epidemics of particular disease in terms of modifications in the parasite. Thus we have had a close study of types and strains of bacteria, of the products of bacterial growth, and of immunity reactions.

It can scarcely be said that these modern methods have enabled the occurrence of epidemics, the bacterial cause of which is known, to be explained much more fully than in the case of other diseases, the parasitic causes of which remain still undiscovered.

Some further explanation of the seasonal periodicity of certain diseases, of epidemic waves and other phenomena which occur seems necessary, and there has recently been some revival of the idea of "epidemic constitutions," whilst climatic and meteorological conditions are believed by others to have a dominant influence. Gill¹ has reviewed the various theories of the past, and points out why, in his opinion, the statistical method of epidemiological research, dealing as it must mainly with figures of mortality, cannot be expected of itself to give answers to the problems involved, although statistical methods cannot be dispensed with. He evidently considers that much more accurate data are needed, and

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says that the application of certain modern methods of statistical analysis to crude statistics of doubtful accuracy is comparable to the use of a razor to cut faggots.

Of recent years our knowledge of epidemiological problems has been reinforced by practical experience in applying sanitary measures (*e.g.*, in regard to malaria, by dealing with breeding-places of mosquitoes) and by the work in experimental epidemiology of Topley, Flexner, Lynch, Amoss and Webster, also by such work as that of Dudley⁵ on diphtheria.

Gill puts forward a theory, which he calls the "quantum" theory, viz., that all epidemic manifestations are essentially the outcome of loss of equilibrium between the dose of toxin and the degree of resistance, or between infection and immunity, and claims that the conclusions reached by Topley as the result of experimental study of mice and by Dudley in his study of human epidemics of diphtheria are almost identical with his theory.

His theory assumes that the principles applicable in the case of the individual apply also to the community.

As a sudden depression of communal immunity is less likely to occur than a sudden increase in amount of infection, Gill believes that circumstances conducing to sudden increase of the infective quantum play a predominant part in determining epidemic explosions.

Four factors are concerned in the mechanism of infection :—

- (1) Reservoir of infection.
- (2) Parasite factor.
- (3) Immunity factor.
- (4) Transmission factor.

The last is of predominant importance in determining the ultimate character of communal disease.

It is clear that diseases due to organisms which are so delicate as to survive separation from a human host for only a short period, and which are transmitted only by close contact, are far less likely to infect large masses of the community in a short space of time than infections transmitted in other ways, such as influenza, plague, smallpox, malaria and cholera, which are capable of world-wide diffusion in great pandemics.

Nevertheless, in connection with venereal diseases, we find some of the characteristics of more typical epidemic

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diseases, *e.g.*, wave form, variations in virulence, seasonal incidence, special incidence upon certain age groups, etc. Particularly is this true of syphilis. But syphilis, like tuberculosis, differs from the acute infectious diseases. These have short incubation periods, sharp acute attack, followed, if death does not occur, by convalescence and complete, or apparently complete, recovery, the whole process lasting for a matter of a few weeks. Syphilis and tuberculosis are examples of more chronic infective processes, manifesting themselves in a variety of forms, often taking years to cure, and with a liability for the disease-producing parasite to lie dormant in the system after the disease has become quiescent or apparently cured, and yet capable of producing, later in life, fresh manifestations of disease, possibly of a different character from the primary.

If epidemic periodicity should occur in such diseases it might be expected that the wave periods would be slow and lengthened out. In the case of tuberculosis several observers believe that such wave periods exist and that the wave cycle may need perhaps hundreds of years for its development.

In the case of syphilis possibly some such periodicity, involving slow changes in virulence or in type of disease manifestation, occurs, although it must be acknowledged that evidence is wanting on which to come to any decided opinion.

It is certain, however, that syphilis does occur at times in epidemic form, involving the infection of large numbers of people with a form of disease showing extraordinary virulence, a great variety of severe manifestations and a considerable proportion of fatal terminations.

The most remarkable instance on record of this kind is the outbreak at the end of the fifteenth century.

I suppose few occurrences in the history of medicine have provoked more acute differences of opinion. So far as I can gather syphilologists are mainly of opinion that syphilis appearing in Europe at the end of the fifteenth century was a new disease so far as Europe was concerned, and that it was introduced from the new world by the sailors of Columbus on their return to Spain in 1493. Epidemiologists, on the other hand, seem mostly to have little doubt that syphilis existed in the old world long before the time of Columbus, and that the epidemic in

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question was merely the blazing up in a virulent form of a disease which had been smouldering for years previously and had been obscured from notice from the fact that its manifestations (less severe probably in type and virulence) had been included under the generic name of Lepra. Medical historians have been inclined to the same view.

In one of the most recent books on the History of Medicine by Singer⁴ appears the following passage :—

“ During the Middle Ages there had smouldered in various districts an obscure disease, sometimes more or less dimly distinguished under various specific names, but most frequently confused with leprosy. Towards the end of the fifteenth century this disease, which was still imperfectly distinguished in men's minds from leprosy, broke out in epidemic and virulent form all over Europe. It caused great destruction of life and developed everywhere as a problem of national importance. Various titles were given it, such as ‘ pox,’ ‘ the French disease,’ ‘ the Spanish disorder.’ Only tardily was it recognised that the disease was usually of venereal origin.”

I confess that both on *a priori* grounds and on the evidence adduced I have not been able to feel satisfied with the conclusion that the disease was introduced to Europe by Columbus and his sailors.

The account given by Creighton,⁶ when dealing with the subject of leprosy, appears to me to make it quite clear that although real leprosy did exist in Great Britain even before the fourteenth century, syphilis also existed, and that the remote effects of syphilis were classed as leprous manifestations. Another writer implies that the leper houses of London were really founded for syphilis when it became epidemic.

As indicated previously, it would seem probable that a disease whose mode of transmission involved such close personal contact had evolved at an early stage of man's existence and had been present in Europe and Asia long before the fifteenth century.

According to some authors, a perfect description of chancres and syphilitic lesions of the skin and mucous membranes is found in Chinese literature, some of it relating to a period 2,000 B.C., whilst a Japanese book of the ninth century is stated to contain a full description of syphilis in all its forms, and to indicate that the relation

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of the constitutional effects of syphilis with the local sore was recognised.

From our general knowledge of epidemics also it appears to me that the period of time between the landing of Columbus and the recognition of a widely diffused and virulent disease was too short to justify the belief that the disease had only been introduced in March, 1493, and that the whole history is more consistent with the theory of a gradual increase of incidence of an existing disease already tending to exhibit increased virulence. The mass movements of population associated with the invasion of Italy by French troops and the conditions of social and communal life at the time were favourable both to increased incidence and increased virulence, the process finally culminating in an explosive outbreak in Italy and in other countries.

The contemporary evidence of medical men, so far as I know, with the exception of Ruy Diaz de Isla, who definitely considered the outbreak in Barcelona in 1493 a new disease and attributed it to the new world, is against the supposition that it was a novel disease. Ten tractates on syphilis published by physicians between 1495 and 1498 have recently been reprinted.* The writers evidently saw nothing novel in the disease they described except increased severity. (One of these physicians identified syphilis with the "Ignis Persicus" of the ancients.)

On the assumption that this view is correct some allusions in the writings of Hippocrates and Rhazes may be perhaps considered as applying to syphilis, and the description of leprosy in Leviticus xiii. may include some of the manifestations of syphilis. The different species of leprosy mentioned are included under the general name "bahereth," "bright spot;" (1) bahereth bohak, the common leprosy, a form not rendering the person affected by it unclean; (2) bahereth libanah, "bright white"; (3) bahereth keha, dark or dusky. The second and third varieties were described as "venom" or "the plague," and were considered dreadfully contagious.

Fox⁷ says that the diagnosis between leprosy and syphilis is not always easy even at the present day. He saw a case of tertiary syphilis which had been treated in South Africa for several years as a case of leprosy.

* See references in *British Medical Journal* of May 21st, 1927.

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Several writers consider that the plague of Baal-peor, in which 24,000 Israelites perished (Numbers xxv. 8), was syphilis. In any case there seems little doubt that it was a venereal disease, acquired by the Israelites through taking part in the licentious orgies connected with the worship of Chemosh. It is interesting as an account of how a virulent outbreak can arise when newcomers are brought into contact with an infected community. According to the record the Israelites had been wandering in the desert for forty years before pitching their tents in the plains of Moab. A new generation had sprung up, presumably never exposed to infection, at least from outside their own community, and when they came into contact with the disease, which apparently affected the Moabites in a comparatively mild form, the result was in the Israelites an outbreak of a virulent and fatal form. Joshua xxii. 17 suggests that the disease abated its virulence, but lingered among the Israelites for some time.

The conditions described in the 38th Psalm are also considered to have been syphilitic, and the writer of Proverbs offers frequent warnings of the dangers of consorting with "the strange women."

The association of the outbreak of great epidemics with mass movements of population is well established. Migrations, pilgrimages, crusades, wars of invasion have been accompanied by disastrous epidemics of infectious diseases of various types (plague, cholera, typhoid fever, etc.).

Clemow⁸ says that movements of mankind are amongst the most powerful influences in distribution of disease. On innumerable occasions emigrants, travellers and explorers have brought small-pox, syphilis and other diseases to countries, islands and isolated communities. He also refers to the annual movements of Russian peasants in search of work as aiding the spread of syphilis and ophthalmia.

The only large scale epidemic of syphilis of which we have records is that already referred to which occurred at the end of the fifteenth century. Whatever view is taken as to the original source of infection, there seems no doubt whatever that its wide distribution and its virulence were associated with the invasion of Italy by the mercenaries of Charles VIII. A large part of his force

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were Swiss, another part were Gascons. The accounts indicate that in this outbreak the disease was malignant in its severity, and it would seem to have been far more readily communicable by innocent contact than syphilis is nowadays. Hence, perhaps, the reluctance of contemporary physicians to consider it in essence a venereal disease.

But the manners and customs of the time, the lack of personal cleanliness, the promiscuous way in which beds were shared, and drinking vessels, table utensils, etc., used without cleansing, would assist its spread otherwise than by sexual intercourse.

The return of the soldiers of Charles VIII. from Italy was no doubt responsible for the extension of this virulent form of syphilis to other countries in Europe.

There is little doubt that it spread to England and that the epidemic was of a severe type in the last two or three years of the fifteenth and the early part of the sixteenth century. It is extraordinary, therefore, that the writings of the English physicians of the time are silent about it. This reticence contrasted strongly with the attention devoted to the subject in Continental medical literature.

References, however, from other sources indicate that the epidemic invasion did not spare Great Britain. (For these I am indebted to Creighton's "History of Epidemics.")

In 1497 the Borough of Aberdeen made a regulation "for the eschevin of the infermity cumm out of Franche" charging 'licht weman' to decist fra thar vices and syne of venerie." A proclamation of September 22nd, 1497, of James IV. at Edinburgh, referred to procedure "for the eschewing of the greit appearand danger of the Infection of his Leiges fra this contagious sickness callit the *Grand gor*." Infected persons were removed to the island of Inch Keith in the Firth of Forth. In 1503 an entry was made in the book of the Privy Purse expenses of Elizabeth of York, Queen of Henry VII., as to a sum of forty shillings paid on behalf of John Pertriche. "Of this" 20s. was "payed to a surgeon which heled him of the Frenche pox." In 1506 the suppression of the stews on the Bankside in Southwark may possibly have been dictated by the desire to limit the spread of the epidemic. Bernard André makes an oblique reference to the matter

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in his *Annals of Henry VII.* Mentioning the sweating sickness of 1508, he says it occurred first in England twenty-four years previously and was "followed by a far more detestable malady . . . a wasting pox which still vexes many eminent men."

The original epidemic is supposed to have become much mitigated in extent and virulence by about 1530, but it is possible that the disease in its most virulent form did not affect England to the same extent as other countries during the first thirty years. William Clowes was the first medical writer in England to deal with the disease. In 1579 he published a revised treatise on the *Morbus Gallicus*, dedicating it to the Society of the Barbers and Chirurgions, to whom the first edition had been offered three years previously. He referred to it as a "sickness very lothsome, odious, troublesome and dangerous, which spreadeth itself throughout all England and overfloweth as I thinke the whole world."

According to Clowes, St. Bartholomew's Hospital, to which he was surgeon, was three parts occupied by patients suffering from this malady.

"It is wonderfull," he says, "to consider how huge multitudes there be of such as be infected with it. . . . In the Hospitall of Saint Bartholomew in London, there hath bene cured of this disease by me, and three (3) others, within this fyve years, to the number of one thousand and more. I speak nothing of Saint Thomas Hospital and other howses about this Citye, wherein an infinite multitude are dayly in cure."

The severity of the disease and its association with military operations are indicated in the reference made by Melville,⁹ who says that in Setubal, during Alva's war in 1579-80, venereal infections assumed such a malignant form that 5,000 penises were amputated.

Melville also states that in the year 1706, when the Anglo-Portuguese Army was encamped near Madrid, there were 6,000 cases of venereal disease in hospitals, of whom the greater part died.

In the Peninsular War 100 years later the British Army suffered severely; many were mutilated by disease. Melville quotes Inspector-General Ferguson as stating that there were more in four years in Portugal than in the hospitals of England for the last century. The disease in the English soldiers was very intractable to

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mercury. With the natives, on the contrary, it was mild and curable by topical treatment alone or wearing itself out.

There was some increase in syphilis in England after the South African War and after the Great War, but no indications of a very severe type of infection.

After the Great War a much greater increase in syphilis seems to have been experienced in Russia than elsewhere. Gantt¹⁰ states that in 1923 doctors from north-western Russia reported that 95 per cent. of the population of their districts were syphilitic, and Dr. Semasko in 1925 stated that although syphilis had greatly decreased throughout Russia, there were still some places where 80 per cent. of the people were infected.

Lack of means of treatment, particularly arsenobenzol compounds and absence of V.D. clinics, were alleged to account partly for this excessive incidence, but it is admitted that overcrowding and filth contributed to the increase. As in the outbreaks in the fifteenth and sixteenth centuries, conditions of overcrowding and carelessness in matters of personal hygiene resulted in a considerable proportion of infection arising otherwise than by sexual contact. Cases were seen with primary chancre in the nose, etc., and whole families were infected by ordinary contact under the extreme conditions of filth.

From another report it would appear that in some villages 45 per cent. of the inhabitants were affected, and in these about 90 per cent. of the infections were extra-genital.

Besides the great epidemic of the fifteenth and sixteenth centuries and the others mentioned above in connection with wars, there have been parallel cases on a minor scale of epidemics of syphilis of specially severe type occurring by the introduction of a comparatively mild type of infection among unsophisticated communities. Reference is made by Creighton to such outbreaks about the Baltic and the Adriatic.

In 1778 syphilis was introduced by Captain Cook's crew to the Hawaiian Islands. It spread rapidly, assumed a severe form and was blamed for the depopulation of the islands. It is now said to have worn itself out.

The phenomenon of the increased severity of disease when there is contact of different races does not necessarily connote that one or the other race is free from syphilitic infection.

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The evidence mentioned above that English soldiers in Portugal during the Peninsular War acquired a severe type of syphilis whilst amongst the natives the disease was comparatively mild, has parallels in other observations. It is said that in China syphilis is mild among the natives but severe amongst foreigners, and the same is stated with regard to Europeans becoming infected in Uganda.

Again, quite recently an increase in the number of fresh infections of syphilis presenting themselves at the Hôpital St. Louis in Paris was attributed partly to invasion of foreign immigrants. In this Hospital 34 per cent. of the inmates of the male wards were foreigners or Colonial natives. It was stated that the proportion of foreign patients was also high in other big industrial centres and ports.

The antiquity of gonorrhœa is generally acknowledged even by those who consider syphilis a new disease. The "running issue" mentioned in Leviticus xv. is accepted as gonorrhœa, and it is interesting to note the scrupulous precautions as to cleanliness enjoined by that great Medical Officer of Health, Moses, in order to prevent infection of others.

It is curious that, notwithstanding this early knowledge of gonorrhœa, the idea persisted for a considerable period that syphilis and gonorrhœa were the same disease.

I am not aware of any record of great epidemics of gonorrhœa, or even of localised outbreaks of a highly virulent type. It is probable, however, that in the conditions of life in the Middle Ages a considerable amount of destructive ophthalmia may have been due to gonorrhœal infection, but in the absence of knowledge of the connection with gonorrhœa it is not surprising that full evidence is wanting.

In the same way, no doubt, local outbreaks of vulvovaginitis occurred from time to time, and were probably much more frequent than at present in view of the overcrowding, promiscuity and lack of hygienic precautions formerly existing. Even now, with all our knowledge of the danger of infection and the need of scrupulous attention to hygienic precautions, small outbreaks of vulvovaginitis occur, due to the common use by healthy and infected of towels, etc. An example is reported by

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Porter¹¹ from South Africa. In 1924 seventeen girls between six and ten years old, living in an exceptionally well-administered home, were notified as suffering from gonorrhœal vulvo-vaginitis, confirmed bacteriologically.

The source was a girl of eleven admitted to the home a fortnight previous to the outbreak who was found suffering from a profuse gonorrhœal discharge, and was discovered to have had relations with men. The home possessed a sufficiency of small slipper-baths, each child had her own towel, and one or more attendants were present during the bathing, but the possibility of children bathing in common could not be excluded, and Porter formed the opinion that the infection was spread in this manner.

The history of outbreaks of syphilis rising to a high pitch of virulence and then subsiding to a stage of a comparatively mild infection corresponds with the sequence of events in connection with other infectious diseases. In such cases we find an epidemic starting with a few mild and perhaps anomalous cases of the disease, then passing on to a stage in which the type of disease is more severe, considerable numbers are affected, and mortality is high. Then the cases gradually dwindle and the epidemic phase is over.

The dying out of an epidemic is sometimes explained as due to exhaustion of the susceptible material; the periodicity of measles, for example, is explained by the time taken for the growing up of a fresh crop of susceptible children.

But recent work suggests some doubt whether the phenomena observed can be fully explained by natural immunity in a section of the population along with acquired immunity in those who have had the disease and survived.

The problem of immunity is a very complex one, and we are only on the threshold of our knowledge as to the factors concerned in its production. The question of immunity in connection with syphilis is particularly puzzling.

Rosenau¹² confirms the opinion of other observers that there is no natural immunity to this disease; all are susceptible, but the severity of cases varies either owing to the virulence of the strain, the amount of infection, or variations in individual resistance.

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Neisser's experiments on monkeys led him to believe that acquired immunity in syphilis depends upon foci of syphilis somewhere in the body. No worker has succeeded in producing active immunity to syphilis, either in man, monkeys or rabbits, whatever antigen has been employed. Nor has immunisation been effected or the course of a syphilitic infection modified by use of a product derived from cultures of spirochætes or from syphilitic tissue. If antibodies are produced in syphilis it is doubtful if they have anything to do with recovery from the disease or the production of resistance to the disease.

If there is no individual absolute resistance (except in those who have acquired resistance through an attack of the disease), it is difficult to explain what appears to be a partial racial or communal resistance leading to a mitigation in severity of the disease in a country where syphilis has long prevailed, or how to account for the reports of severe attacks of syphilis experienced by English soldiers in the Peninsular War (and coming from a syphilised country) in Portugal, where the natives experienced only mild attacks.

There is also another phenomenon to be considered: an attack of syphilis was supposed to protect against further infection. But recent experiments reported by Mestchersky and Bagdanoff¹³ suggest that "surinfection" is possible, and that absolute immunity does not exist even during an attack of syphilis. They produced, by inoculation, lesions identical with spontaneous syphilis in patients already suffering from syphilis in various stages from primary sore to tabes.

If these conclusions are correct it is less to be wondered at that a patient who has been promptly and efficiently treated with arsenobenzol preparations for an attack of syphilis until his Wassermann reaction remains permanently negative can be reinfected in the normal way.

Andrewes² expressed the view that personal immunity in syphilis given by an attack was not true immunity, but only latency.

The work of Topley¹⁴ in experimental epidemiology suggests that this question of latency is a much more important factor in connection with infectious diseases than has hitherto been realised, and that it may have an important bearing on individual and communal immunity.

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His experiments have convinced him that clinically recognisable cases of disease form only a fraction of the infected individuals of the host species. In examining adequate samples of (a) cases of disease, (b) contacts with atypical symptoms, (c) healthy contacts, and (d) healthy non-contacts, the specific parasite is found in descending order of frequency. But within an epidemic area investigation may show equal values for the carrier rate in healthy contacts and non-contacts, so that there is no reason to suppose that contact with a clinically recognisable case of disease is the main mode of infection leading to the carrier state.

The possibility of latency in syphilis has long been recognised as regards women. We know that women who have never presented clinical signs of syphilis may give birth to syphilitic infants and may have a positive Wassermann reaction.

Warthin³ has suggested that there is a distinct sex difference between men and women, and that, particularly during the child-bearing period, a woman has some immunity which prevents the development of the ordinary symptoms of syphilis, the disease remaining latent, but capable of transmission to the offspring. He considers that syphilis is probably as frequent in women as in men, but more often missed. The primary sore especially tends to be overlooked. He believes that the liver is more frequently the seat of syphilitic localisation in women than in men, and that the ovary, heart and aorta are less likely to be affected in women than the heart, aorta and testis in men. Also there is less liability to affections of the central nervous system in women.

Bory¹⁵ suggests the possibility of the existence in women of unrecognised but contagious syphilis evading the strictest clinical observation, and asks whether it is possible for an apparently non-syphilitic woman to convey infection to a man?

It has been observed by another writer that, especially in pregnancy, there seems to be in women some principle exerting an inhibitory effect, taking off the edge of the virulence, and causing a state of *endo-syphilis* where clinical signs are absent. Montgomery has suggested that this may be associated with more active secretion of iodothylin.

But it is apparently not only in women that the disease

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may be "latent." Kolle¹⁶ states that it is difficult to believe that all cases of syphilis originate from contact with cases of open infection. He emphasises the well-known fact that many patients are found to be syphilitic during the course of routine examination who never suspected it themselves; this applies especially to patients with disease of the nervous or arterial system. Formerly we used to suspect the truthfulness of such patients who denied all suspicious symptoms of syphilis during their previous history. It is possible that such cases are becoming more common, and it is conceivable that this increase in latency may be associated with the other phenomenon of the rarity of the more severe clinical manifestations even in untreated cases.

Kolle suggests that a large number of patients with latent syphilis have become infected without ever developing primary manifestations, and that they are in reality chronic carriers of the disease, and that they may prove infective in much the same way as an apparently healthy person who is a "typhoid" carrier. He thinks such persons may carry living spirochætes on their mucosæ without showing any evidence of disease.

The suggestion that the *Treponema pallidum* is only one stage of the life-cycle of the organism of syphilis has now been accepted by Levaditi¹⁷ and others, and this "resting" stage of the parasite may possibly be the culprit in endo-syphilis and in those forms of the disease in the central nervous system in which no organism can be found. The resting forms are considered to be more resisting to chemo-therapeutic agents than the spirochætal vegetative forms.

It is possible, if this theory is correct, that some of the perplexing problems of syphilis may be solved when we obtain greater knowledge of the life-history of the parasite of syphilis.

Possibly, for instance, the communal resistance to syphilis leading to a mild type of disease may be due to what has been called "latent immunisation" by sub-minimal doses of the virus, perhaps in its resting form, and that this process might go on in a community until the strain of virus became much attenuated. The occurrence of conditions reducing the general resistance of the population, or the introduction from outside of a virulent strain, might then be sufficient to start an outbreak of a

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severe type. Thus we can visualise an epidemic cycle in syphilis as with other infectious diseases.

Changes in type and severity of disease are well known. Scarlet fever and smallpox are modern instances, and in syphilis it is the subject of frequent remark that we do not see now the severe type of case which was common enough thirty years ago.

In the fight against syphilis and gonorrhœa we are faced with great difficulties. In the case of the gonococcus we have an organism extremely delicate when outside the body, yet capable of entrenching itself within the body in a way which makes successful attack very difficult, whilst the carrier of the germ may readily infect others. In the case of gonorrhœa, however, there are gleams of hope that one day we may discover a vaccine which will reach the gonococcus in its lair and destroy it.

In the case of syphilis the foe seems even more wily and resourceful. As Stokes says, the symbiosis between man and parasite in the case of syphilis is almost too perfect to break up. *Spirochaeta pallida* is not sitting around awaiting for us to kill it. It is a living organism, intent on living and reproducing. We thought we had secured a deadly weapon when the arsenobenzol preparations were introduced, and undoubtedly these substances have given the enemy a shrewd blow. But it appears as if certain strains of the organism are being evolved capable of very considerable resistance to arsenic, and what Stokes calls the "inveterate arsphenamine-fast-relapser" is becoming something of a problem.

In conclusion, many of the considerations I have mentioned should warn us not to be too sanguine or to consider the conquest of venereal diseases a foregone conclusion, not to be too sure that diminution in severe or open syphilis is entirely the fruit of our special measures unaided by other factors the existence of which we dimly perceive in our study of epidemic disease. Similarly we must not rashly assume that such progress as has been made in combating venereal disease is a permanent gain which can be securely held.

Nevertheless, avoiding rash and vainglorious assumptions of victory, we should not be discouraged even if fresh phases seem to deny our hopes. The experience of other infectious diseases encourages us to anticipate that, notwithstanding ups and downs, by perseverance in the

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painful and laborious search for fresh knowledge as to the nature of man and of his parasites and their various reactions to their environments, we may ultimately find the secret which will give us the final mastery over this scourge of humanity.

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